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(FILE 'HOME' ENTERED AT 16:13:52 ON 16 APR 2003)

FILE 'MEDLINE, CAPLUS, BIOSIS, SCISEARCH' ENTERED AT 16:14:05 ON 16 APR 2003

L1 100667 S BACTERIOPHAGE  
L2 14977 S (VARIABLE(W)REGION OR V) (6A)ANTIBODY  
L3 117 S L1 AND L2  
L4 40 S L1(S)L2  
L5 25 DUP REM L4 (15 DUPLICATES REMOVED)

=> d au ti so ab 1-25 l5

L5 ANSWER 1 OF 25 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.  
AU Mardh, Sven (1)  
TI Recombinant phages.  
SO Official Gazette of the United States Patent and Trademark Office Patents,  
(Dec. 24 2002) Vol. 1265, No. 4, pp. No Pagination.  
<http://www.uspto.gov/web/menu/patdata.html>. e-file.  
ISSN: 0098-1133.

AB The present invention relates to **bacteriophages** for use in the treatment or prophylaxis of bacterial infections, especially mucosal bacterial infections such as *Helicobacter pylori* infections, in particular, it relates to modified filamentous **bacteriophages**, e.g. M13 phages, for such use, which **bacteriophages** present at the surface a recombinant protein comprising (i) a first component derived from a **bacteriophage** surface protein; and (ii) a second component comprising **variable region** sequences of an **antibody** to provide a bacterial antigen binding site, said second component rendering said **bacteriophage** capable of binding to and thereby inhibiting growth of bacterial cells involved in the etiology of said infection.

L5 ANSWER 2 OF 25 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.  
AU Lopez, Osvaldo (1); Wylie, Dwane E.; Wagner, Fred W.  
TI Mercury binding polypeptides and nucleotides coding therefore.  
SO Official Gazette of the United States Patent and Trademark Office Patents,  
(Oct. 26, 1999) Vol. 1227, No. 4, pp. No pagination. e-file.  
ISSN: 0098-1133.

AB Metal binding polypeptides which include an amino acid sequence coding for a **variable region** of a monoclonal **antibody** which immunoreacts with a mercury cation and nucleotides which include a nucleic acid sequence coding for the variable region are provided. The invention is also directed to fusion proteins which include a phage coat protein or portion thereof and the monoclonal **antibody** heavy chain **variable region**. The invention also provides **bacteriophages** which include the fusion protein in their coat. In addition, methods for detecting, removing, adding, or neutralizing mercuric cations in biological or inanimate systems through the use of the mercury binding polypeptides are provided.

L5 ANSWER 3 OF 25 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE  
1

AU Gao, Changshou; Mao, Shenlan; Lo, Chih-Hung L.; Wirsching, Peter; Lerner, Richard A. (1); Janda, Kim D. (1)  
TI Making artificial antibodies: A format for phage display of combinatorial heterodimeric arrays.  
SO Proceedings of the National Academy of Sciences of the United States of America, (May 25, 1999) Vol. 96, No. 11, pp. 6025-6030.  
ISSN: 0027-8424.  
AB The gene VII protein (pVII) and gene IX protein (pIX) are associated closely on the surface of filamentous **bacteriophage** that is

opposite of the end harboring the widely exploited pIII protein. We developed a phagemid format wherein **antibody** heavy- and light-chain **variable regions** were fused to the amino termini of pVII and pIX, respectively. Significantly, the fusion proteins interacted to form a functional Fv-binding domain on the phage surface. Our approach will be applicable to the display of generic peptide and protein libraries that can form combinatorial heterodimeric arrays. Consequently, it represents a first step toward artificial antibodies and the selection of novel biological activities.

L5 ANSWER 4 OF 25 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 2

AU Nuttall, Stewart D. (1); Rousch, Mat J.M.; Irving, Robert A.; Hufton, Simon E.; Hoogenboom, Hennie R.; Hudson, Peter J.

TI Design and expression of soluble CTLA-4 variable domain as a scaffold for the display of functional polypeptides.

SO Proteins, (Aug. 1, 1999) Vol. 36, No. 2, pp. 217-227.  
ISSN: 0887-3585.

AB We have designed and engineered the human cytotoxic T-lymphocyte associated protein-4 (CTLA-4) variable (V-like) domain to produce a human-based protein scaffold for peptide display. First, to test whether the CTLA-4 CDR-like loops were permissive to loop replacement/insertion we substituted either the CDR1 or CDR3 loop with somatostatin, a 14-residue intra-disulfide-linked neuropeptide. Upon expression as periplasmic-targeted proteins in *Escherichia coli*, molecules with superior solubility characteristics to the wild-type V-domain were produced. These mutations in CTLA-4 ablated binding to its natural ligands CD80 and CD86, whereas binding to a conformation-dependent anti-CTLA-4 monoclonal **antibody** showed that the V-domain framework remained correctly folded. Secondly, to develop a system for library selection, we displayed both wild-type and mutated CTLA-4 proteins on the surface of **bacteriophage** as fusions with the geneIII protein. CTLA-4 displayed on phage bound specifically to immobilized CD80-Ig and CD86-Ig and in one-step panning enriched 5,000 to 2,600-fold respectively over wild-type phage. **Bacteriophage** displaying CTLA-4 with somatostatin in CDR3 (CTLA-4R-Som3) specifically bound somatostatin receptors on transfected CHO-K1 cells preincubated with 1 µg/ml tunicamycin to remove receptor glycosylation. Binding was specific, as 1 µM somatostatin successfully competed with CTLA-4R-Som3. CTLA-4R-Som3 also activated as well as binding preferentially to non-glycosylated receptor subtype Sst4. The ability to substitute CDR-like loops within CTLA-4 will enable design and construction of more complex libraries of single V-like domain binding molecules.

L5 ANSWER 5 OF 25 CAPLUS COPYRIGHT 2003 ACS

IN Mardh, Sven

TI Bacteriophages presenting recombinant surface protein fusion products with bacteria antigen-binding antibody for use in bacterial infection treatment

SO PCT Int. Appl., 34 pp.  
CODEN: PIXXD2

AB The present invention relates to bacteriophages for use in the treatment or prophylaxis of bacterial infections, esp. mucosal bacterial infections such as *Helicobacter pylori* infections. In particular, it relates to modified filamentous **bacteriophages**, e.g., M13 phages, for such use, which **bacteriophages** present at its surface a recombinant protein comprising: (i) a first component derived from a **bacteriophage** surface protein; and (ii) a second component comprising **variable region** sequences of an **antibody** to provide a bacterial antigen binding site, said second component rendering said **bacteriophage** capable of binding to and thereby inhibiting growth of bacterial cells involved in the etiol. of said infection.

L5 ANSWER 6 OF 25 MEDLINE

DUPLICATE 3

- AU Tsumoto K; Nishimiya Y; Kasai N; Ueda H; Nagamune T; Ogasahara K; Yutani K; Tokuhisa K; Matsushima M; Kumagai I
- TI Novel selection method for engineered antibodies using the mechanism of Fv fragment stabilization in the presence of antigen.
- SO PROTEIN ENGINEERING, (1997 Nov) 10 (11) 1311-8.  
Journal code: 8801484. ISSN: 0269-2139.
- AB Although the heavy and light chain domains of some antibody variable region fragments (Fvs) readily dissociate under physiological conditions, the Fvs are stable in the presence of antigen. This 'antigen-driven Fv stabilization mechanism' was applied to the selection of clones with specificity toward target antigens. The results can be summarized as follows. (i) Some of the residues in the heavy chain complementarity determining region 2 (HCDR2) of anti-hen egg white lysozyme (HEL) monoclonal **antibody** HyHEL10 heavy chain **variable region** (VH) were randomized. (ii) The randomized VH fragments of HyHEL10 were displayed on a filamentous **bacteriophage** and mixed with the target antigen, before being applied to a light chain variable region (VL) which was immobilized on microtiter plates and subjected to selection by panning. (iii) After four rounds of panning, four clones that showed significant binding to human lysozyme (hL), which HyHEL10 recognized poorly, were selected from the HCDR2 library. (iv) The soluble Fv fragments selected were expressed in Escherichia coli, purified, and subjected to an inhibition assay of lysozyme enzymatic activities and an isothermal titration calorimetry. These Fv fragments had increased affinity toward hL, and thermodynamic analysis suggested that the reduced entropy loss due to binding by the replacement of residues in HCDR2 resulted in the higher hL binding activity.
- L5 ANSWER 7 OF 25 SCISEARCH COPYRIGHT 2003 ISI (R)
- AU Chung J H (Reprint); Choi S J; Him H J; Kim I J; Choi I H; Lee S D; Yi K S; Suh P G; Ryu S H; Chung H K
- TI Cloning and characterization of cDNAs encoding V-H and V-L of a monoclonal anti-CEA antibody (CEA 79) cross-reactive with NCA-95 and generation of a single-chain Fv molecule (scFv)
- SO MOLECULES AND CELLS, (31 DEC 1997) Vol. 7, No. 6, pp. 816-819.  
Publisher: KOREAN SOC MOLECULAR BIOLOGY, KOREA SCI TECHNOLOGY CENTER, ROOM 815, 635-4 YEOGSAM-DONG KANGNAM-GU, SEOUL 135-703, SOUTH KOREA.  
ISSN: 1016-8478.
- AB We cloned complementary DNA (cDNA) encoding the variable regions of heavy chain (V-H) and of light chain (V-L,) of a monoclonal anti-carcinoembryonic antigen (CEA) antibody cross-reactive with nonspecific cross-reacting antigen-95 (NCA-95), which had been previously prepared and designated as CEA 79 (gamma(2a),,, kappa). From these cDNAs, a phagemid expression vector for the CEA79 single chain variable fragment (scFv) was generated. Enzyme-linked immunosorbent assay (ELISA), competitive ELISAs, and Western blotting confirmed that the scFv displayed on the surface of the **bacteriophage** had retained affinity for CEA and NCA-95. We then determined the nucleotide sequences of the cloned cDNAs for V-H, and V-L,. The sequence analysis revealed that V-H, and V-L, of the CEA 79 **antibody** represent new members of the mouse heavy chain subgroup 'miscellaneous' and the kappa light chain subgroup 'V', respectively.
- L5 ANSWER 8 OF 25 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 4
- AU Denton, G. (1); Sekowski, M.; Spencer, D. I. R.; Hughes, O. D. M.; Murray, A.; Denley, H.; Tendler, S. J. B.; Price, M. R.
- TI Production and characterization of a recombinant anti-MUC1 scFv reactive with human carcinomas.
- SO British Journal of Cancer, (1997) Vol. 76, No. 5, pp. 614-621.  
ISSN: 0007-0920.
- AB Recombinant single-chain fragments (scFv) of the murine anti-MUC1 monoclonal antibody C595 have been produced using the original hybridoma cells as a source of variable heavy (V-H)- and variable light (V

-L)-chain-encoding **antibody** genes. The use of the polymerase chain reaction (PCR), **bacteriophage** (phage) display technology and gene expression systems in *E. coli* has led to the production of soluble C595 scFv. The scFv has been purified from the bacterial supernatant by peptide epitope affinity chromatography, leading to the recovery of immunoreactive C595 scFv, which was similar in activity to the C595 parent antibody. Analysis by DNA sequencing, SDS-PAGE and Western blotting has demonstrated the integrity of the scFv, while ELISA, FACScan analysis, fluorescence quenching, quantitative immunoreactivity experiments and immunohistochemistry confirm that the activity of the scFv compares favourably with that of the parent antibody. The retention of binding activity to MUC1 antigen on human bladder and breast carcinoma tissue specimens illustrates the potential application of this novel product as an immunodiagnostic and immunotherapeutic reagent.

L5 ANSWER 9 OF 25 CAPLUS COPYRIGHT 2003 ACS

AU Sodoyer, Regis; Peubez, Isabelle; Pion, Corinne; Dubayle, Joseline; Jacquemot, Paul; Geoffroy, Frederique; Even, Jos; Aujame, Luc

TI Full-scale "naive" human antibody repertoires assembled from VH and VL variable regions

SO Human Antibodies (1997), 8(1), 37-42

CODEN: HUANFP; ISSN: 1093-2607

AB Very large "naive" human antibody repertoires have been obtained from RT-PCR cloned VH and VL variable regions. They are used as starting material for the assembly of medium sized combinatorial libraries or so called multicombinatorial libraries. In nonimmunized individuals Ig mRNAs are poorly expressed, which can be a serious limitation for cloning efficiency. To overcome this problem two complementary strategies have been used: a nonspecific polyclonal activation of B cells, and a secondary PCR amplification technique to ensure recovery of Ig messengers in large amt. and without introducing any bias.

L5 ANSWER 10 OF 25 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 5

AU Popov, Sergei; Hubbard, J. Gregory; Ward, E. Sally (1)

TI A novel and efficient route for the isolation of antibodies that recognise T cell receptor V-alpha-s.

SO Molecular Immunology, (1996) Vol. 33, No. 6, pp. 493-502.

ISSN: 0161-5890.

AB Studies of the T cell repertoire have been hindered by the lack of **antibodies** that recognise V region families, particularly for V-alpha regions. In this report, single chain Fv (scFv) fragments have been isolated that recognise both recombinant V-alpha-s and native V-alpha-s on the surface of T cells. Mice have been immunized with purified soluble T cell receptors (TCRs) and antibody heavy and light chain variable domain (VH and VL, respectively) genes isolated from splenocytes using the polymerase chain reaction (PCR). The VH and VL genes have been assembled as scFv gene libraries and a **bacteriophage** display system used to isolate scFvs that recognise a soluble V-alpha. Five scFvs have been purified and characterized in detail using enzyme-linked immunosorbent assays (ELISAs) and flow cytometry. Three of these five scFvs recognise native V-alpha-s on the surface of T cell hybridomas. This method therefore offers a rapid route to the generation of scFvs that recognise native TCRs and can readily be extended to the production of anti-human TCR antibodies for use in therapy and diagnosis.

L5 ANSWER 11 OF 25 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 6

AU Wagner, Simon D.; Gross, Gideon; Cook, Graham P.; Davies, Sarah L.; Neuberger, Michael S.

TI Antibody expression from the core region of the human IgH locus reconstructed in transgenic mice using bacteriophage P1 clones

SO Genomics (1996), 35(3), 405-414

CODEN: GNMCEP; ISSN: 0888-7543

AB Mice carrying transgenic human Ig gene miniloci can be used for the prodn.

of human monoclonal antibodies. The human variable region (V) gene segments in these miniloci undergo productive rearrangement in mouse lymphoid tissue to yield a population of B lymphocytes expressing a repertoire of antibodies. Many of the miniloci studied to date have included only a small no. of germline gene segments in an artificially compact configuration. Here the authors describe the use of the bacteriophage P1 cloning system to create mice carrying the core region of the human Ig heavy chain (IgH) locus. Three P1 clones carrying overlapping regions of the human IgH locus (spanning the five JH-proximal VH segments, the entire DH and JH clusters, and the C.mu. and C.delta. const. regions) were injected into mouse eggs and appear to have reconstituted the core region of the locus (>180 kb) following homologous recombination with each other. While this trans-locus yielded a titer of serum Ig similar to that obtained with a smaller plasmid-based minilocus, the P1-based locus gave rise to substantially greater diversification by somatic hypermutation. Such diversification is important for obtaining high-affinity antibodies. The results show the usefulness of the P1 system in facilitating the manipulation and recreation of large transgenes.

- L5 ANSWER 12 OF 25 CAPLUS COPYRIGHT 2003 ACS  
 IN Lopez, Osvaldo; Wylie, Dwane E.; Wagner, Fred W.  
 TI Preparation and expression cloning of mercury-binding monoclonal antibody sequences and their use for immunoassays  
 SO PCT Int. Appl., 107 pp.  
 CODEN: PIXXD2
- AB Metal-binding polypeptides and nucleic acids are provided which include an amino acid sequence coding for a variable region of a monoclonal antibody which immunoreacts with a mercury cation and a nucleotide sequence coding for the variable region. Fusion proteins and **bacteriophages** can include a phage coat protein or portion thereof and the monoclonal **antibody heavy chain variable region**. In addn., methods are described for detecting, removing, adding, or neutralizing Hg2+ in biol. or inanimate systems through the use of the mercury-binding polypeptides. Thus, hybridomas antibodies were produced with the spleen cells of BALB/c mouse that had received multiple injections of Hg2+ reacted with glutathione covalently bound to keyhole limpet hemocyanin. Seven hybridoma antibodies immunoreactive with glutathione-Hg2+ and specific for Hg2+ were cloned, PCR amplified, and the Fd and .kappa. regions sequenced. ELISA assay utilizing BSA-glutathione added to polyvinyl chloride microtiter plates enabled detection of Hg2+ in a concn. as low as 10-9 M (0.2 ppb) with antibody IF10. Phagmid vectors are constructed to fuse the antibody Fd chain with the C-terminal domain of the coat protein cpIII of phage M13.
- L5 ANSWER 13 OF 25 CAPLUS COPYRIGHT 2003 ACS  
 IN Kurosawa, Yoshikazu; Ito, Wataru  
 TI Methods for selecting genes for antibodies using antibodies-display bacteriophage particles  
 SO Jpn. Kokai Tokkyo Koho, 26 pp.  
 CODEN: JKXXAF
- AB A chimeric gene X-(Y)m-(Z)n (X=gene for **variable regions** of an **antibody**; Y=gene for expressing polypeptides on the surface of **bacteriophage**; Z=gene for Fc-binding polypeptide; m,l=0, 1) is described to improve the selection of the gene for the antibody. Bacteriophage display vectors expressing the target antibody on their surface can be recovered and enriched with antigens immobilized on resins. The enriched vectors then re-infect Escherichia coli for the prepn. of the antibody. Plasmid pM13Fv contg. the genes encoding Fv of a monoclonal antibody to hen egg lysozyme, .DELTA.cpIII (the C-terminal fragment of a linear bacteriophage coat protein III or cpIII), and protein A was constructed. M13Fv bacteriophage particles infected with plasmid pM13Fv expressed VH and VL on their surface. The method can be used for the recombinant prepn. of monoclonal or polyclonal antibody that exhibits

affinity to the target antigen.

- L5 ANSWER 14 OF 25 MEDLINE DUPLICATE 7  
AU Nilsson B  
TI Antibody engineering.  
SO CURRENT OPINION IN STRUCTURAL BIOLOGY, (1995 Aug) 5 (4) 450-6. Ref: 77  
Journal code: 9107784. ISSN: 0959-440X.
- AB Antibody engineering has been an extremely intensive research area for many years. Recent achievements discussed in this review include: (i) significant improvements in the field of selection of antigen-specific antibody fragments on **bacteriophages**; (ii) new structural work, in particular using NMR; (iii) the cloning of essentially the complete set of human VH genes; (iv) the use of **antibodies** to catalyze complicated chemical reactions; and (v) novel **antibody** fusion proteins to potentiate immune therapy. An interesting new development is the replacement of antibodies with more stable protein scaffolds for many future biotechnological applications.
- L5 ANSWER 15 OF 25 SCISEARCH COPYRIGHT 2003 ISI (R)  
AU FILPULA D (Reprint); ROLLENCE M; ESSIG N; NAGLE J; ACHARI A; LEE T  
TI ENGINEERING OF IMMUNOGLOBULIN FC AND SINGLE-CHAIN FV PROTEINS IN ESCHERICHIA-COLI  
SO ACS SYMPOSIUM SERIES, (1995) Vol. 604, pp. 70-85.  
ISSN: 0097-6156.
- AB The field of antibody engineering encompasses the investigation and redesign of constant domain associated effector functions, as well as the intensive current research on variable domain associated antigen-binding sites. We have investigated the potential of E. coli expression of single-chain Fv and Fc proteins to both provide model systems and practical reagents for antibody effector region interactions. We shall first review the current status of single-chain Fv protein engineering. A selected single-chain Fv protein with human-IgM C-mu specificity has been constructed and characterized in our laboratory. The **variable region** genes of anti-mu monoclonal **antibody** DA4.4 were isolated and an engineered sFv version of this antibody expressed in E. coli was shown to be an IgM-specific binding protein. A simple screening method was developed for protein-protein interactions between recombinant C-H-producing E. coli and C-H-binding proteins displayed on the surface of **bacteriophage** M13. This method, which allows facile engineering and recovery of recombinant gem products, provides a model system for the characterization and designed modification of antibody effector domains.
- L5 ANSWER 16 OF 25 SCISEARCH COPYRIGHT 2003 ISI (R)  
AU WINTER G (Reprint); GRIFFITHS A D; HAWKINS R E; HOOGENBOOM H R  
TI MAKING ANTIBODIES BY PHAGE DISPLAY TECHNOLOGY  
SO ANNUAL REVIEW OF IMMUNOLOGY, (1994) Vol. 12, pp. 433-455.  
ISSN: 0732-0582.
- AB Antibody fragments of predetermined binding specificity have recently been constructed from repertoires of **antibody V** genes, bypassing hybridoma technology and even immunization. The V gene repertoires are harvested from populations of lymphocytes, or assembled in vitro, and cloned for display of associated heavy and light chain variable domains on the surface of filamentous **bacteriophage**. Rare phage are selected from the repertoire by binding to antigen; soluble antibody fragments are expressed from infected bacteria; and the affinity of binding of selected antibodies is improved by mutation. The process mimics immune selection, and antibodies with many different binding specificities have been isolated from the same phage repertoire. Thus human antibody fragments have been isolated with specificities against both foreign and self antigens, including haptens, carbohydrates, secreted and cell surface proteins, viral coat proteins, and intracellular antigens from the lumen of the endoplasmic reticulum and the nucleus. Such antibodies have potential as reagents for research and in therapy.

- L5 ANSWER 17 OF 25 SCISEARCH COPYRIGHT 2003 ISI (R)  
 AU SANDHU J S (Reprint)  
 TI PROTEIN ENGINEERING OF ANTIBODIES  
 SO CRITICAL REVIEWS IN BIOTECHNOLOGY, (1992) Vol. 12, No. 5-6, pp. 437-462.  
 ISSN: 0738-8551.
- AB This article reviews the technical advances in antibody engineering and the clinical applications of these molecules. Recombinant DNA technology facilitates the construction and expression of engineered antibodies. These novel molecules are designed to meet specific applications. Although genomic and cDNA cloning have been used widely in the past to isolate the relevant **antibody V** domains, at present, the PCR-based cloning is the preferred system. Bacterial and mammalian expression systems are used commonly for the production of antibodies, antibody fragments, and antibody fusion proteins. A range of chimeric **antibodies** with murine V domains joined to C regions from human and other species have been produced and found to exhibit the expected binding characteristics and effector functions. Humanized antibodies have been developed to minimize the HAMA response, and bifunctional immunoglobulins are being used in tumor therapy and diagnosis. Single chain antibodies and fusion proteins with antibody specificities joined to nonimmunoglobulin sequences provide a source of antibody-like molecules with novel properties. The potential applications of minimal recognition units and antigenized antibodies are described. Combinatorial libraries produced in **bacteriophage** present an alternative to hybridomas for the production of antibodies with the desired antigen binding specificities. Future developments in this field are discussed also.
- L5 ANSWER 18 OF 25 MEDLINE DUPLICATE 8  
 AU McCafferty J; Griffiths A D; Winter G; Chiswell D J  
 TI Phage antibodies: filamentous phage displaying antibody variable domains.  
 SO NATURE, (1990 Dec 6) 348 (6301) 552-4.  
 Journal code: 0410462. ISSN: 0028-0836.
- AB New ways of making antibodies have recently been demonstrated using gene technology. Immunoglobulin variable (V) genes are amplified from hybridomas or B cells using the polymerase chain reaction, and cloned into expression vectors. Soluble antibody fragments secreted from bacteria are then screened for binding activities. Screening of V genes would, however, be revolutionized if they could be expressed on the surface of bacteriophage. Phage carrying V genes that encode binding activities could then be selected directly with antigen. Here we show that complete **antibody V** domains can be displayed on the surface of fd **bacteriophage**, that the phage bind specifically to antigen and that rare phage (one in a million) can be isolated after affinity chromatography.
- L5 ANSWER 19 OF 25 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.  
 AU VALERIE K; GREEN A P; DE RIEL J K; HENDERSON E E  
 TI TRANSIENT AND STABLE COMPLEMENTATION OF UV REPAIR IN XERODERMA PIGMENTOSUM CELLS BY THE DEN-V GENE OF BACTERIOPHAGE T4.  
 SO CANCER RES, (1987) 47 (11), 2967-2971.  
 CODEN: CNREA8. ISSN: 0008-5472.
- AB In this paper we report both transient and stable complementation of pyrimidine dimer repair in xeroderma pigmentosum cells by the denV gene of **bacteriophage** T4, coding for endonuclease V, a dimer-specific DNA glycosylase. Cotransfectin with pRSVdenV in SV40-transformed XP12RO(M1) cells (complementation group A) restored transient expression of an indicator plasmid (pRSVcat) bearing a UV-inactivated chloramphenicol acetyltransferase (cat) gene. In addition, XP12RO(M1) clones stably transformed by pRSVdenV-SVgpt expressed transient chloramphenicol acetyltransferase activity when transfected with UV-inactivated pRSVcat plasmid. These clones also showed partial restoration of colony forming ability and excision repair synthesis after UV irradiation. Immunofluorescence, using an endonuclease V polyclonal

**antibody**, showed the presence of the phage glycosylase in stably transformed xeroderma pigmentosum cells. The cotransfection assay affords a rapid, sensitive procedure to screen for functional cloned DNA repair genes and to test mutant cells for the deficiency of specific steps in DNA repair, such as incision.

- L5 ANSWER 20 OF 25 MEDLINE DUPLICATE 9  
AU Valerie K; Fronko G; Long W; Henderson E E; Nilsson B; Uhlen M; de Riel J K  
TI Production and detection of coliphage T4 endonuclease V polyclonal and monoclonal antibodies using staphylococcal protein-A hybrid proteins.  
SO GENE, (1987) 58 (1) 99-107.  
Journal code: 7706761. ISSN: 0378-1119.  
AB To facilitate the production of **antibodies** against endonuclease V, a pyrimidine dimer-specific DNA glycosylase produced in **bacteriophage** T4-infected *Escherichia coli*, we constructed plasmids containing protein-A-endonuclease V fusion genes under control of the *E. coli* tac promoter. Induction with isopropyl-beta-D-thiogalactopyranoside produced large amounts of fusion proteins, which could easily be purified on human IgG agarose columns. The affinity-purified fusion proteins were injected into rabbits and mice to produce polyclonal and monoclonal antibodies, and also used for the screening of the monoclonal antibodies. These antibodies recognized endonuclease V on immunoblots, and also inhibited the DNA-glycosylase activity in vitro. Epitope mapping of monoclonal antibodies showed that they all (6/6) recognized determinants in the C-half of endonuclease V. A convenient way to detect primary antibodies on nitrocellulose was also developed using a crude protein extract containing protein-A-beta-galactosidase fusion protein and subsequent detection with a mixture of dyes.
- L5 ANSWER 21 OF 25 MEDLINE DUPLICATE 10  
AU Lloyd R S; Augustine M L  
TI Cloning and expression of the 3' portion of the T4 denV gene as a lacZ fusion gene.  
SO MUTATION RESEARCH, (1986 Mar) 165 (2) 89-100.  
Journal code: 0400763. ISSN: 0027-5107.  
AB Polyclonal **antibodies** have been raised against endonuclease V from the **bacteriophage** T4. This rabbit serum, from which endemic *E. coli* antibodies have been removed, reacts with a single protein from T4-infected *E. coli* with a molecular weight of 16078 dalton. It was confirmed that these antibodies were directed against endonuclease V through the inhibition of the pyrimidine dimer specific nicking activity of endonuclease V in an in vitro nicking assay. A phage lambda gt11 T4 dC DNA library was screened for phage which produced a beta-galactosidase-endonuclease V fusion protein. Immunopositive clones were detected at a frequency of 0.25% of the plaques in the library. Restriction enzyme analyses of the DNA from 45 of these phage showed that all contained a 1.8 kb T4 EcoRI fragment which had been inserted within lambda gt11 in a single orientation. Western analysis of proteins which were produced from an induction of lysogens made from these phage reveals a single fusion protein band with a molecular weight slightly larger than native beta-galactosidase.
- L5 ANSWER 22 OF 25 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.  
AU HIGGINS D A; GATRILL A J  
TI A COMPARISON OF THE ANTIBODY RESPONSES OF BADGERS MELES-MELES AND RABBITS ORYCTOLAGUS-CUNICULUS TO SOME COMMON ANTIGENS.  
SO INT ARCH ALLERGY APPL IMMUNOL, (1984) 75 (3), 219-226.  
CODEN: IAAAAM. ISSN: 0020-5915.  
AB The primary and secondary antibody responses of rabbits and badgers [the badger is highly susceptible to tuberculosis] were compared after i.v. inoculation of inactivated influenza A virus, sheep erythrocytes (SRBC), bovine serum albumin (BSA) or **bacteriophage** .PHI.X174. BSA was



also given as a primary injection by i.m. route in solution or in Freund's incomplete or complete adjuvant, followed by an i.v. secondary inoculation without adjuvant. **Antibody** responses were monitored by hemagglutination inhibition and neutralization tests for influenza virus; direct and antiglobulin hemagglutination tests for SRBC; indirect hemagglutination test and the Farr method for antigen-binding capacity (ABC) for BSA; neutralization of .PHI.X174. Rabbits gave good responses to all antigens, but the response of badgers was generally poor. After i.v. administration, badgers gave a good response only to .PHI.X174, but even then they produced less antibody than rabbits receiving 100 times less antigen; the immune elimination of phage was more rapid and antibody appeared about 48 h earlier in rabbits than in badgers. Administration i.m. of BSA and the use of adjuvants improved the badgers' response, with greatest improvement in ABC. Badgers display relatively poor immune responses to a variety of antigens.

- L5 ANSWER 23 OF 25 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.  
 AU OCHS H D; WEDGWOOD R J; FRANK M M; HELLER S R; HOSEA S W  
 TI THE ROLE OF COMPLEMENT IN THE INDUCTION OF ANTIBODY RESPONSES.  
 SO CLIN EXP IMMUNOL, (1983) 53 (1), 208-216.  
 CODEN: CEXIAL. ISSN: 0009-9104.
- AB To determine the effect of complement on the normal antibody response to T cell-dependent antigens, normal and C4 [complement component 4] deficient guinea pigs were immunized with **bacteriophage** .PHI.X 174. Following primary immunization with a standard dose (2 .times. 109 PFU/kg) given i.v., C4 deficient guinea-pigs produced less **antibody** than normal guinea pigs and were unable to maintain measurable antibody levels. Following secondary immunization, antigen clearance of C4 deficient guinea pigs was delayed and the subsequent antibody response was delayed and the subsequent antibody response was identical to their primary response without amplification or isotype switch. Increased antigen dose and administration of antigen in adjuvants into footpads improved the responses but did not make them normal. The primary and secondary responses became essentially normal, when small amounts of normal guinea pig serum were given to the deficient animals at the time of the primary (but not the secondary) immunization. The contribution of complement to the mature humoral immune response is apparently related to activation of C3. Antigen evidently initiates a primary immune response. The resultant antigen-antibody complexes interact with complement and are then non-specifically trapped by C3 receptors on dendritic cells. B cells and macrophages. Antigen is selectively accumulated within the lymphoid organs and in turn captures antigen specific B cells by interaction of the trapped antigen with antigen specific sIg [surface Ig]. The approximation of specific lymphoid cells, macrophages and antigen permits generation of specific memory cells and ensures prompt, mature antibody response on subsequent antigen exposure.
- L5 ANSWER 24 OF 25 MEDLINE DUPLICATE 11  
 AU Finkelstein M S; Uhr J W  
 TI **Antibody** formation. V. The avidity of gamma-M and gamma-G guinea pig antibodies to **bacteriophage** phi-x 174.  
 SO JOURNAL OF IMMUNOLOGY, (1966 Nov) 97 (5) 565-76.  
 Journal code: 2985117R. ISSN: 0022-1767.
- L5 ANSWER 25 OF 25 CAPLUS COPYRIGHT 2003 ACS  
 AU Seaman, Edna; Levine, Lawrence; Vunakis, Helen Van  
 TI Immunochemical studies on **bacteriophage** deoxyribonucleic acid. V. Specificity of **antibodies** to deoxyribonucleic acid after immunization with methylated bovine serum albumin deoxyribonucleic acid complexes  
 SO Biochemistry (1965), 4(10), 2091-8  
 AB cf. CA 62, 16768h. The serologic specificities of antibodies produced in rabbits by immunization with methylated serum albumin complexes of T4 DNA, T4 apurinic acid, and T4 DNA in which 50% of the guanine had been

destroyed during irradiation with visible light in the presence of methylene blue have been studied. All of the antisera contained antibodies directed primarily toward the .alpha.-glucosyl hydroxymethylcytidylic acid of the T4 DNA. All of the antisera with the exception of antiphotooxidized T4 DNA, showed specificity for T-even coliphage DNA. The antiphotooxidized T4 DNA contained addnl. antibodies which reacted with heterologous DNA lacking glucosylhydroxymethylcytidylic acid. This cross reaction was used to measure the thermally produced helix-to-random-coil transition of 5 DNA preps. varying in their guanine and cytosine content from 37 to 72%. These antibodies were inhibited most effectively by deoxyguanosine and deoxycytidine monophosphates and less effectively by deoxyadenosine and thymidine monophosphates. Among the mono-, di-, and tricytosine derivs. tested by hapten inhibition, cytidyl-3',5'-cytidylic acid was the most effective inhibitor. Removal of the terminal phosphates decreased its effectiveness as an inhibitor. In addn., the antiphotooxidized T4 DNA contained antibodies directed toward the product which resulted from the exposure of DNA to visible light in the presence of methylene blue.

=> s (treat? or prophylaxis) (8a)bacteria?(3a)infection  
L6 9839 (TREAT? OR PROPHYLAXIS) (8A) BACTERIA?(3A) INFECTION

=> s l5 and l6  
L7 2 L5 AND L6

=> d bib ab 1-2 l7

L7 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2003 ACS

AN 1997:542514 CAPLUS

DN 127:186628

TI Bacteriophages presenting recombinant surface protein fusion products with **bacteria** antigen-binding antibody for use in **bacterial infection treatment**

IN Mardh, Sven

PA Mardh, Sven, Swed.

SO PCT Int. Appl., 34 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9729185	A1	19970814	WO 1997-SE172	19970205
	W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
	SE 9600434	A	19970807	SE 1996-434	19960206
	SE 506771	C2	19980209		
	CA 2244792	AA	19970814	CA 1997-2244792	19970205
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	AU 712767	B2	19991118		
	EP 889955	A1	19990113	EP 1997-902815	19970205
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI			
	CN 1210558	A	19990310	CN 1997-192116	19970205
	JP 2000505648	T2	20000516	JP 1997-528446	19970205
	NO 9803456	A	19981006	NO 1998-3456	19980727
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PRAI	SE 1996-434	A	19960206		
	WO 1997-SE172	W	19970205		
	US 1998-117798	B3	19980806		

AB The present invention relates to bacteriophages for use in the **treatment or prophylaxis of bacterial infections**, esp. mucosal **bacterial infections** such as *Helicobacter pylori* infections. In particular, it relates to modified filamentous **bacteriophages**, e.g., M13 phages, for such use, which **bacteriophages** present at its surface a recombinant protein comprising: (i) a first component derived from a **bacteriophage** surface protein; and (ii) a second component comprising **variable region** sequences of an **antibody** to provide a bacterial antigen binding site, said second component rendering said **bacteriophage** capable of binding to and thereby inhibiting growth of bacterial cells involved in the etiol. of said infection.

L7 ANSWER 2 OF 2 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.  
 AN 2003:92654 BIOSIS  
 DN PREV200300092654  
 TI Recombinant phages.  
 AU Mardh, Sven (1)  
 CS (1) S-582 25, Linkoping, Sweden Sweden  
 PI US 6497874 December 24, 2002  
 SO Official Gazette of the United States Patent and Trademark Office Patents, (Dec. 24 2002) Vol. 1265, No. 4, pp. No Pagination.  
<http://www.uspto.gov/web/menu/patdata.html>. e-file.  
 ISSN: 0098-1133.

DT Patent

LA English

AB The present invention relates to **bacteriophages** for use in the **treatment or prophylaxis of bacterial infections**, especially mucosal **bacterial infections** such as *Helicobacter pylori* infections, in particular, it relates to modified filamentous **bacteriophages**, e.g. M13 phages, for such use, which **bacteriophages** present at the surface a recombinant protein comprising (i) a first component derived from a **bacteriophage** surface protein; and (ii) a second component comprising **variable region** sequences of an **antibody** to provide a bacterial antigen binding site, said second component rendering said **bacteriophage** capable of binding to and thereby inhibiting growth of bacterial cells involved in the etiology of said infection.